HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Albutein® 20% safely and effectively. See full prescribing information for Albutein® 20%.

Albutein® 20% [Albumin (Human) U.S.P.] sterile, aqueous solution for single dose intravenous administration
Initial U.S. Approval: 1978

INDICATIONS AND USAGE

Albumin (Human) U.S.P., Albutein® 20% Solution is indicated (1):
- For treatment of hypovolemic shock.
- As an adjunct in hemodialysis for patients undergoing long-term dialysis or for those patients who are fluid-overloaded and cannot tolerate substantial volumes of salt solution for therapy of shock or hypotension.
- In cardiopulmonary bypass procedures; however, the optimum regimen of fluids has not been established.

Conditions in which Albutein® 20% **MAY BE** indicated:
- Adult respiratory distress syndrome (ARDS).
- Major injury or surgery resulting in increased albumin loss or inadequate synthesis.
- Acute nephrosis not responding to cyclophosphamide or steroid therapy. Steroid therapy may increase edema which may respond to combined therapy of albumin with a diuretic.
- Acute liver failure or ascites where the therapeutic use is regulated by the individual circumstances.

Unless the pathologic condition responsible for hypoalbuminemia can be corrected, administration of albumin can afford only symptomatic relief. There is **NO** valid reason for the use of albumin as an intravenous nutrient.

DOSAGE AND ADMINISTRATION

Albutein® 20% is administered intravenously. The total dosage will vary with the individual. In adults, an initial infusion of 100 mL is suggested. Additional amounts may be administered as clinically indicated.
- When an administration set is used (2.1)
- When an administration set is not used (2.2)

DOSAGE FORMS AND STRENGTHS

Albutein® 20% is a sterile, aqueous solution for single dose intravenous administration containing 20% human albumin (weight/volume), provided in the following presentations: (3)
- 10.0 g albumin/50 mL single dose vial
- 20.0 g albumin/100 mL single dose vial

CONTRAINDICATIONS

- Patients with severe anemia or cardiac failure in the presence of normal or increased intravascular volume (4)
- Patients with a history of allergic reactions to albumin (4)

WARNINGS AND PRECAUTIONS

- Risk of infectious agents (5.1)
- Patients with low cardiac reserve (5.2)

ADVERSE REACTIONS

The most common adverse reactions include fever and chills, rash, nausea, vomiting, tachycardia and hypotension (6)
To report SUSPECTED ADVERSE REACTIONS, contact Grifols Biologicals Inc. at 1-888-GRIFOLS (1-888-474-3657) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

To report SUSPECTED ADVERSE REACTIONS, contact at or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

USE IN SPECIFIC POPULATIONS

- Unknown whether can cause fetal harm or affect reproduction capacity (8.1)
- The pediatric use has not been clinically evaluated (8.4)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 07/2008

FULL PRESCRIBING INFORMATION: CONTENTS *

*** Sections or subsections omitted from the full prescribing information are not listed**

FULL PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

Albumin (Human) U.S.P., Albutein® 20% Solution is indicated:

1. For treatment of hypovolemic shock.[1,2]
2. As an adjunct in hemodialysis for patients undergoing long-term dialysis or for those patients who are fluid-overloaded and cannot tolerate substantial volumes of salt solution for therapy of shock or hypotension.[3]
3. In cardiopulmonary bypass procedures; however, the optimum regimen of fluids has not been established.

Conditions in which Albutein® 20% **MAY BE** indicated:

- Adult respiratory distress syndrome (ARDS).[3,4]
- Major injury or surgery resulting in increased albumin loss or inadequate synthesis.[3,5]
- Acute nephrosis not responding to cyclophosphamide or steroid therapy. Steroid therapy may increase edema which may respond to combined therapy of albumin with a diuretic.[3]
- Acute liver failure or ascites where the therapeutic use is regulated by the individual circumstances.[3]

Unless the pathologic condition responsible for hypoalbuminemia can be corrected, administration of albumin can afford only symptomatic relief. There is **NO** valid reason for the use of albumin as an intravenous nutrient.

2. DOSAGE AND ADMINISTRATION

Albutein® 20% is administered intravenously. The total dosage will vary with the individual. In adults, an initial infusion of 100 mL is suggested. Additional amounts may be administered as clinically indicated.

In the treatment of the patient in shock with greatly reduced blood volume, Albutein® 20% may be administered as rapidly as necessary in order to improve the clinical condition and restore normal blood volume. This may be repeated in 15-30 minutes if the initial dose fails to prove adequate. In the patient with a slightly low or normal blood volume, the rate of administration should be 1 mL per minute.

If dilution of Albutein® 20% is clinically desirable, compatible diluents include sterile 0.9% Sodium Chloride solution or sterile 5% Dextrose in Water.[6]

DIRECTIONS FOR USE: (50 mL and 100 mL)

2.1 When an Administration Set is Used

Flip off plastic cap on top of the vial and expose rubber stopper. Cleanse exposed rubber stopper with suitable germicidal solution, being sure to remove any excess. Observe aseptic technique and prepare sterile intravenous equipment as follows:

1. Close clamp on administration set.
2. With bottle upright, squeeze drip chamber, thrust piercing pin straight through stopper center. Do not twist or angle.
3. Immediately invert bottle, release drip chamber to automatically establish proper fluid level in drip chamber (half full).
4. Attach infusion set to administration set, open clamp and allow solution to expel air from tubing and needle, then close clamp.
5. Make venipuncture and adjust flow.
6. Discard all administration equipment after use. Discard any unused contents.

2.2 When an Administration Set is Not Used

Flip off plastic cap on top of the vial and expose rubber stopper. Cleanse exposed rubber stopper with suitable germicidal solution, being sure to remove any excess. Observe aseptic technique and prepare sterile intravenous equipment as follows:

1. Using aseptic technique, attach filter needle to a sterile disposable plastic syringe.
2. Insert filter needle into Albutein® 20%.
3. Aspirate Albutein® 20% from the vial into the syringe.

4. Remove and discard the filter needle from the syringe.

5. Attach desired size needle to syringe.

6. Discard all administration equipment after use. Discard any unused contents.

3. DOSAGE FORMS AND STRENGTHS

Albutein® 20% is a sterile, aqueous solution for single dose intravenous administration containing 20% human albumin (weight/volume). It is available in the following presentations:

- 10.0 g albumin/50 mL single dose vial.
- 20.0 g albumin/100 mL single dose vial.

4. CONTRAINDICATIONS

Albutein® 20% is contraindicated in patients with severe anemia or cardiac failure in the presence of normal or increased intravascular volume.

The use of Albutein® 20% is contraindicated in patients with a history of allergic reactions to albumin.

5. WARNINGS AND PRECAUTIONS

5.1 Warnings

Following reports that there exists a risk of potentially fatal hemolysis and acute renal failure from the inappropriate use of Sterile Water for Injection as a diluent for Albumin (Human)[7], if dilution is required, acceptable diluents include 0.9% Sodium Chloride or 5% Dextrose in Water.[6]

Albutein® 20% is made from pooled human plasma. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases, including a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD). Although no cases of transmission of viral diseases or CJD have ever been identified for albumin, the risk of infectious agents cannot be totally eliminated. The physician should weigh the risks and benefits of the use of this product and should discuss these with the patient.

Solutions of Albutein® 20% should not be used if they appear turbid or if there is sediment in the bottle. Do not begin administration more than 4 hours after the container has been entered. Discard unused portion.

5.2 Precautions

Albutein® 20% should be administered with caution to patients with low cardiac reserve.

Rapid infusion may cause vascular overload with resultant pulmonary edema. Patients should be closely monitored for signs of increased venous pressure.

A rapid rise in blood pressure following infusion necessitates careful observation of injured or postoperative patients to detect and treat severed blood vessels that may not have bled at a lower pressure.

Patients with marked dehydration require administration of additional fluids. Albutein® 20% may be administered with the usual dextrose and saline intravenous solutions. However, certain solutions containing protein hydrolysates or alcohol must not be infused through the same administration set in conjunction with Albutein® 20% since these combinations may cause the proteins to precipitate. See also **PATIENT COUNSELING INFORMATION (17).**

6. ADVERSE REACTIONS

The most common adverse reactions include fever and chills, rash, nausea, vomiting, tachycardia and hypotension. Should an adverse reaction occur, slow or stop the infusion for a short period of time which may result in the disappearance of the symptoms. If administration has been stopped and the patient requires additional Albutein® 20%, material from a different lot should be used.

Albutein® 20%, particularly if administered rapidly, may result in vascular overload with resultant pulmonary edema.

To report SUSPECTED ADVERSE REACTIONS, contact Grifols Biologicals Inc. at 1-888-GRIFOLS (1-888-474-3657) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with Albutein® 20%. It is also not known whether Albutein® 20% can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Albutein® 20% should be given to a pregnant woman only if clearly needed.

8.4 Pediatric Use

Albutein® 20% is indicated in conjunction with exchange transfusion in the treatment of neonatal hyperbilirubinemia. The pediatric use of Albutein® 20% has not been clinically evaluated. The dosage will vary with the clinical state and body weight of the individual. Typically, a dose one-quarter to one-half the adult dose may be administered, or dosage may be calculated on the basis of 0.6 to 1.0 gram per kilogram of body weight (3 to 5 mL of Albutein® 20%). For jaundiced infants suffering from hemolytic disease of the newborn, the appropriate dose for binding of free serum bilirubin is 1 gram per kilogram of body weight which may be administered during the procedure.[8] The usual rate of administration in children should be one-quarter the adult rate. Therefore, physicians should weigh the risks and benefits of the use of Albutein® 20% in the pediatric population.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

11. DESCRIPTION

Albutein® 20% is a sterile, aqueous solution for single dose intravenous administration containing 20% human albumin (weight/volume). Albutein® 20% is prepared by a cold alcohol fractionation method from pooled human plasma obtained from venous blood. The product is stabilized with 0.08 millimole sodium caprylate and 0.08 millimole sodium acetyltryptophanate per gram of albumin. Albutein® 20% is osmotically equivalent to four times its volume of normal human plasma. Albutein® 20% contains 130-160 milliequivalents of sodium ion per liter and has a pH of 7.0 ± 0.3. The aluminum content of the solution is not more than 200 micrograms per liter during the shelf life of the product. The product contains no preservatives.

Albutein® 20% is heated at 60 °C for ten hours. No positive assertion can be made, however, that this heat treatment completely destroys the causative agents of viral hepatitis.

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

There are no known cases of viral hepatitis which have resulted from the administration of Albutein® 20%. Albumin is a highly soluble, globular protein (MW 66,500), accounting for 70-80% of the colloid osmotic pressure of plasma. Therefore, it is important in regulating the osmotic pressure of plasma.[1,3] Albutein® 20% supplies the oncotic equivalent of approximately 4 times its volume of human plasma. It will increase the circulating plasma volume by an amount approximately 2.5 times the volume infused within 15 minutes, if the recipient is adequately hydrated.[9] This extra fluid reduces hemoconcentration and decreases blood viscosity. The degree and duration of volume expansion depend upon the initial blood volume. When treating patients with diminished blood volume, the effect of infused albumin may persist for many hours. The hemodilution lasts for a shorter time when albumin is administered to individuals with normal blood volume.

Albumin is also a transport protein and binds naturally occurring, therapeutic, and toxic materials in the circulation.[1]

Albumin is distributed throughout the extracellular water and more than 60% of the body albumin pool is located in the extravascular fluid compartment. The total body albumin in a 70 kg man is approximately 320 g. Albumin has a circulating life span of 15-20 days, with a turnover of approximately 15 g per day.[3]

15. REFERENCES

1. Finlayson, J.S., Albumin Products *Semin Thromb Hemo*, 6:85-120, 1980.
2. Hauser, C.J., et. al., Oxygen Transport Responses to Colloids and Crystalloids in Critically Ill Surgical Patients, *Surg Gyn Obs*, 150:811-816, June 1980.
3. Tullis, J.L., Albumin: 1. Background and Use. 2. Guidelines for Clinical Use. *JAMA* 237:355-360, 460-463, 1977.
4. Shoemaker, W.C., et. al., Comparison of the Relative Effectiveness of Colloids and Crystalloids in Emergency Resuscitation, *Am J Surg*, 142:73-84, July 1981.
5. Peters, T., Jr., Serum Albumin in: *The Plasma Proteins*, 2nd Ed., Putnam F.W. (ed), New York, Academic Press, 1:133-181, 1975.
6. Albumin Human. In AHFS Drug Information, 1144-1146, 1998.
7. Data on File, FDA.
8. Tsao, Y.C., Yu, V.Y.H., Albumin in the Management of Neonatal Hyperbilirubinemia, *Arch Dis Childhood*, 47:250-256, 1972.
9. Janeway, C.A., Human Serum Albumin: Historical Review in *Proceedings of the Workshop on Albumin*, Sgouris, J.T. and Rene A. (eds), DHEW Publication No. (NIH) 76-925, Washington, D.C., U.S. Government Printing Office, 1976, pp. 3-21.

16. HOW SUPPLIED/STORAGE AND HANDLING

Albutein® 20% is supplied as a sterile, aqueous solution for single dose intravenous administration containing 20% human albumin (weight/volume). It is available in the following vial sizes:

- 50 mL vial Albutein® 20% (NDC 68516-5215-1).
- 100 mL vial Albutein® 20% (NDC 68516-5215-2).

Storage

Albutein® 20% is stable for three years provided that storage temperature does not exceed 30 °C. Protect from freezing.

17. PATIENT COUNSELING INFORMATION

The most common adverse reactions include fever and chills, rash, nausea, vomiting, tachycardia and hypotension. Depending on the severity of the reaction, patients should be advised to discontinue use of the product and contact their physician and/or seek immediate emergency care.

Albutein® 20% should be administered with caution to patients with low cardiac reserve.

Rapid infusion may cause vascular overload with resultant pulmonary edema. Patients should be closely monitored for signs of increased venous pressure.

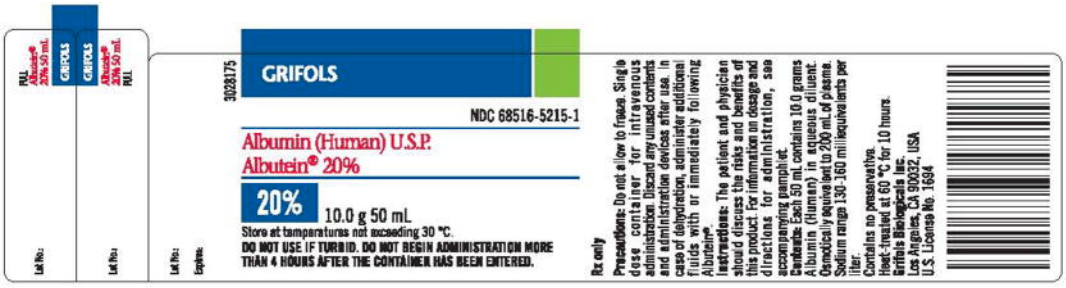
A rapid rise in blood pressure following infusion necessitates careful observation of injured or postoperative patients to detect and treat severed blood vessels that may not have bled at a lower pressure.

Patients with marked dehydration require administration of additional fluids. Albutein® 20% may be administered with the usual dextrose and saline intravenous solutions. However, solutions containing protein hydrolysates or alcohol must not be infused through the same administration set in conjunction with Albutein® 20% since these combinations may cause the proteins to precipitate. See also **WARNINGS AND PRECAUTIONS (5.2).**

Manufactured and Distributed by:
Grifols Biologicals Inc.
Los Angeles, CA 90032, U.S.A.
U. S. License No. 1694
DATE OF REVISION: 07/2008
3028178

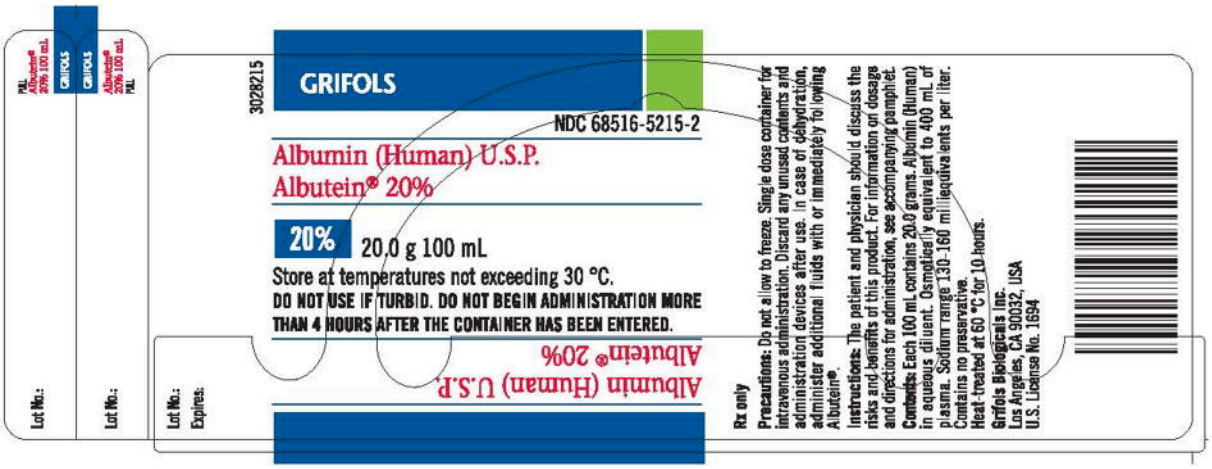
PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 50 ML VIAL
GRIFOLS
NDC 68516-5215-1
Albumin (Human) U.S.P.

Albutein® 20%
20% 10.0 g 50 mL
Store at temperatures not exceeding 30 °C.
DO NOT USE IF TURBID. DO NOT BEGIN ADMINISTRATION MORE THAN 4 HOURS AFTER THE CONTAINER HAS BEEN ENTERED.



PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 100 ML VIAL
GRIFOLS
NDC 68516-5215-2
Albumin (Human) U.S.P.

Albutein® 20%
20% 20.0 g 100 mL
Store at temperatures not exceeding 30 °C.
DO NOT USE IF TURBID. DO NOT BEGIN ADMINISTRATION MORE THAN 4 HOURS AFTER THE CONTAINER HAS BEEN ENTERED.



PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 50 ML CARTON
GRIFOLS
NDC 68516-5215-1
Albumin (Human) U.S.P.

Albutein® 20%
Solution 10.0 g 50 mL
20%
Store at temperatures not exceeding 30 °C.

PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 100 ML CARTON
GRIFOLS
NDC 68516-5215-2
Albumin (Human) U.S.P.
Albutein® 20%
Solution 20.0 g 100 mL
20%
Store at temperatures not exceeding 30 °C.


GRIFOLS
NDC 68516-5215-2
Albumin (Human) U.S.P.
Albutein® 20%
Solution 20.0 g 100 mL
20%
Store at temperatures not exceeding 30 °C.
6851652152
3028177
GRIFOLS
Contents:
One 100 mL vial Albumin (Human) U.S.P. Albutein®. Each 100 mL contains 20.0 grams Albumin (Human) in aqueous diluent.
Osmotically equivalent to 400 mL of plasma.
Sodium range 130-160 milliequivalents per liter.
Stabilized with 0.08 millimole sodium caprylate and 0.08 millimole sodium acetyltryptophanate per gram of albumin.
Contains no preservative.
Heat-treated at 60 °C for 10 hours.
Grifols Biologicals Inc.
Los Angeles, CA 90032, USA
U.S. License No. 1694
GRIFOLS
NDC 68516-5215-2
Albumin (Human) U.S.P.
Albutein® 20%
Solution 20.0 g 100 mL
20%
Store at temperatures not exceeding 30 °C.
3028177
GRIFOLS
Rx only
Precautions:
Do not allow to freeze.
Single dose container for intravenous administration.
Discard any unused contents and administration devices after use.
In case of dehydration, administer additional fluids with or immediately following Albutein®.
Instructions:
The patient and physician should discuss the risks and benefits of this product. For information on dosage and directions for administration, see enclosed pamphlet.
DO NOT USE IF TURBID.
DO NOT BEGIN ADMINISTRATION MORE THAN 4 HOURS AFTER THE CONTAINER HAS BEEN ENTERED.